## **REMARKS**

Claims 52-85 are pending. Favorable reconsideration is respectfully requested.

The present invention relates to a method for providing cells with the capacity to produce a protein, the amino acid sequence of which comprises at least one unconventional amino acid, comprising:

- (a) introducing at least one missense mutation in a target codon of a gene encoding a protein required for the growth of the cells, wherein the mutated protein synthesized from the mutated gene is not functional in the cells; and
- (b) culturing the cells obtained in (a) in a culture medium which (1) does not contain a nutrient compensating for the loss of functionality of the mutated protein and (2) contains an unconventional amino acid which restores the functionality of said protein required for growth of the cells, said unconventional amino acid being any amino acid incorportaed in place of the amino acid, which should normally be incorporated at this site with regard to the translated nucleic acid sequence.

See Claim 86.

The rejection of Claims 52-53, 55-72 and 74-85 under 35 U.S.C. §112, second paragraph, is believed to be obviated by the amendment submitted above in part and is, in part, respectfully traversed.

Claim 86 corresponds to Claim 52. Practicing the method steps recited in Claim 86 accomplishes the preamble set forth in that claim.

Claim 101 corresponds to Claim 67 and properly depends from Claim 100.

Claim 103 corresponds to Claim 70. Claim 103 depends directly from Claim 86 and is, therefore, a product-by-process claim.

Claim 118 corresponds to Claim 85. Claim 118 specifies incorporating into the amino acid sequence of the protein an unconventional amino acid containing a functional group, wherein the incorporation is obtained according to the process of Claim 108.

In view of the foregoing, the claims are believed to be definite within the meaning of 35 U.S.C. §112, second paragraph. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 69-72 and 74 under 35 U.S.C. §112, first paragraph, is respectfully traversed.

Claim 69 is cancelled and there is no claim which corresponds to it in the pending Claims 86-118. In addition, the claims which correspond to the claims that depended from Claim 69 now depend from Claim 103.

In addition, as noted at page 4 of the Official Action, the process defined in Claim 86 is fundamentally different from genetic recombination of ARNt-synthetase genes. In fact, it is not required that one have an exact knowledge on the genetic background of the cells in order to implement the invention. Accordingly, the cells are selected for their ability to acquire the capacity to produce proteins which contain at least one unconventional amino acid.

An unconventional amino acid is defined in the specification (see the bottom of page 2) as any amino acid incorporated by ribosomes during the biosynthesis of proteins in place of the amino acid which should normally be incorporated at this site, with regard to the translated nucleic acid sequence. In addition, the present invention provides an alternative approach, where any gene involved in protein synthesis, and not only ARNt-synthetase genes, is likely to be modified insofar as to render possible the incorporation of unconventional amino acids into proteins. In view of these circumstances, the Applicants are

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entitled to the method as claimed and should not be limited to the case of ARNt-synthetase gene mutations, which corresponds to a preferred embodiment of the invention.

In view of the foregoing, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully Submitted,

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